VRB Research Projects (Z01 RS)

No.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 00001-14 VR

Annual Report

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Animal Model Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Carl T. Hansen Geneticist SAS, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.33	.27

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project is designed to develop animal model systems to meet the requirements of a broad spectrum of research programs to include immunology, infectious diseases, parasitology, behavior, neurological disorders, metabolic diseases, and cardiovascular disorders in small animals utilizing the closed breeding groups maintained by the NIH Animal Genetics Resources. The project is collaborative in nature in that all of the breeding programs are carried out internally and the evaluation of the model is performed by the research community. During the year, evaluations were completed on two models, one in the mouse and the other in the rat. A colony of immunocompromised mice was established on the N:NIH outbred background by combining three genes, nude (nu), beige (nu), and X-linked immune defect (xid), all of which affect various components of the immune system. The results of an initial test indicate that mice carrying these genes is a superior model for heterotransplantation of human tumor material to ordinary nude mice which have been previously used for this purpose. In the rat, the SHR/N-cp (corpulent) congenic strain promises to be a useful model for insulin independent diabetes as well as the role that brown fat plays in regulating body temperature. Other mouse and rat models are currently under evaluation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00002-13 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Development of Diets for Laboratory Animals

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J. J. Knapka	Nutritionist	SAS, VRB, DRS
Others:	D. Barnard	Biologist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.6	.6	1.0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A continuing program in laboratory animal nutrition involves study with the most frequently used species of small laboratory animals such as rats, mice, guinea pigs, and rabbits as well as dogs and various species of nonhuman primates. A series of factorial designed feeding trials are used to ascertain the nutrient requirements of the animals of interest and to develop diets with more nearly optimal nutrient concentrations for their growth, reproduction, maintenance, or general health status. This program has resulted in the development of open formula natural ingredient diets for most of the animal species maintained in significant numbers at NIH. The major exception is the dog and plans have been made to initiate studies involving this species. In addition, a major effort is being made to develop a complete diet for marmosets.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00029-07 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Clinical Pathology Studies of Animal Health Conditions

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	E. J. Baas	Chief	CU, ACS, VRB, DRS
Others:	F. J. Judge	Chief	ACS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.5	.3	.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Studies are being conducted to define and characterize spontaneous diseases occurring in the NIH canine colonies. Preliminary clinical investigation has identified some disease problems. Hematological and chemical tests are being performed. The purpose of these investigations is to improve the quality of animals and animal products provided for research and characterize models of disease.

PHS 6040 (Rev. 1/84) GPO 904-917

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00030-07 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Evaluation of Mycobacterium paratuberculosis Bacteria in the Goat

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	M. L. Morin	Chief, PRU	VMSS, VRB, DRS
Others:	L. D. Stuart	Chief, UU	ACS, VRB, CRS
	R. Merkal	Research Veterinarian	NADL

COOPERATING UNITS *(if any)*

National Animal Disease Laboratory
Agriculture Research Service
Ames, Iowa

LAB/BRANCH

Veterinary Resources Branch

SECTION

Veterinary Medicine and Surgery Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.02	.01	.01

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study is designed to determine if a bacterin against Johne's disease will affect the incidence and age of onset of the disease in goats. One-half of the kid goats produced by NIH Animal Center conventional does in 1978 and 1979 were vaccinated at one month of age are being observed for life.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00042 06 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Development of a Standard Strain of Mice for Pertussis Vaccine Bioassays

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

K. P. Smith Geneticist CPS, VRB, DRS

COOPERATING UNITS *(if any)*

Small Animal Section, VRB, DRS, NIH
Pertussis Branch, National Center for Drugs and Biologics, FDA

LAB/BRANCH

Veterinary Resources Branch

SECTION

Comparative Pathology Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.5	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The objective of this project is to develop a standard strain of mice used for pertussis vaccine bioassays. Two lines of mice have been selectively bred for their susceptibility and resistance to sensitization by the histamine sensitizing factor (HSF) of Bordetella pertussis and have been designated HSFS/N and HSFR/N. After 20 generations of selection, the ability to be sensitized by HSF in the HSFS/N line has increased to 70 percent, and in the HSFR has decreased to 0.5 percent. The two lines have been further characterized for 12 biochemical isozymes.

PHS 6040 (Rev. 1/84) GPO 904-917

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00047-06 VR

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 cherecters or less. Title must fit on one line between the borders.)*
Screening Laboratory Animal Diets for Chemical Contamination

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: J. J. Knapka Nutritionist SAS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Small Animal Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.15	.05	.10

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The direct DRS involvement in this program has been discontinued because the administration of the program does not require additional research. The routine monitoring of animal feeds continues but under the direction of the NIH Quality Assurance Branch.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00051-05 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*

Reproduction in Mutant Sheep Used for the Study of Hyperbilirubinemia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	L. D. Stuart	Chief	UU, ACS, VRB, DRS
Others:	D. E. Wildt	Guest Worker	VRB, DRS
	S. C. Kalser	Director	Liver Diseases Prog., DDN, NIAID
	P. K. Chakraborty	Head	Res. Division, Dept. of OB-GYN, USUHS

COOPERATING UNITS *(if any)*

Digestive Diseases and Nutrition Program, National Institutes of Arthritis, Metabolism and Digestive Diseases.

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.1	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A specific genetic strain of Corriedale sheep is used as an animal model for the study of liver pathophysiology, specifically, hyperbilirubinemia (Dubin-Johnson Syndrome). This project is concerned with increasing the numbers of animals available for research by the controlled breeding of individuals which genetically transmit this character. This project is utilizing what is considered to be the only existing Corriedale sheep homozygotic for this trait. Efforts are being made to obtain both homozygous and heterozygous offspring from these highly inbred individuals. Semen collected artificially from rams is diluted in various cryoprotective extenders and then freeze preserved. This will ensure the long-term availability of male gametes for artificial insemination. Overall, this project allows perpetuation of this specific gene pool and ensures availability of research animals for future investigations of Dubin-Johnson Syndrome and related metabolic disorders.

PHS 6040 (Rev. 1/84)

GPO 904-917

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00065-03 VR

PERIOD COVERED

October 1, 1963 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effect of Diet on Cataract Incidence in Rats with Hereditary Retinal Dystrophy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: J.J. Knapka Nutritionist SAS, VRB, DRS

COOPERATING UNITS *(if any)*

Retinal and Ocular Corrective Tissue Diseases Section
Chemical Branch, NEI

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.6	.1	.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A series of studies designed to identify dietary constituents affecting cataract incidence in rats with hereditary retinal dystrophy are being conducted. Both purified and natural ingredient diets varying in nutrient and ingredient composition are being evaluated. The age of onset and the incidence of cataracts can be influenced by dietary alterations. It appears there is a significant increase in the incidence of cataracts when fish meal is used in purified and natural ingredient diets. Although fish meal contains a considerable amount of calcium, results of studies where graded concentrations of calcium were fed in purified diets did not implicate this as the factor influencing the incidence of cataracts.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00066-03 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Effect of Diet on the Incidence of Stroke in Rats

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: J. J. Knapka Nutritionist SAS, VRB, DRS

COOPERATING UNITS *(if any)*

Biochemical Pharmacology Section, Hypertension-Endocrine Branch
Division of Intramural Research, NHLBI

LAB/BRANCH

Veterinary Resources Branch

SECTION

Small Animal Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	.1	.4

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A series of factorially designed studies were conducted to ascertain the influence of dietary protein and salt in the incidence of stroke in the stroke prone rat strain. The direct involvement of DRS personnel in this project has been discontinued because it was not possible to monitor the blood pressure of test animals as well as could be accomplished by NHLBI.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00067-02 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Hematologic and Serum Chemical Characteristics of Aotus sps.

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigetor.) (Name, title, laboratory, and institute affiliation)*

PI:	D. M. Renquist	Chief	PU, ACS, VRB, DRS
Others:	R. W. Atwell	Bio. Lab. Tech.	PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.2	0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Hematologic and serum chemical characteristics of 120 Aotus monkeys were determined to acquire information which may be useful in the care of these animals. This information may also be useful in determining the usefulness of this species as an animal model. The monkeys were bled every four months for one year. The hematologic and serum chemical characteristics are being statistically analyzed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00068-02 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Zinc Deficiency in S. mystax and its relationship to Wasting Marmoset Syndrome

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. E. Barnard	Biologist	SAS, VRB, DRS
Others:	D. M. Renquist	Unit Chief	PU, ACS, VRB, DRS
	J. J. Knapka	Nutritionist	SAS, VRB, DRS

COOPERATING UNITS *(if any)*

Small Animal Section

LAB/BRANCH

Veterinary Resources Branch

SECTION

Animal Center Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.40	.30	.10

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this study was to determine if the etiology of Wasting Marmoset Syndrome (WMS) is related to zinc deficiency. The clinical symptoms of zinc deficiency and WMS are very similar. It was determined that S. mystax exhibiting signs of WMS were zinc deficient. The study involved feeding two diets to several wasting S. mystax, one diet was supplemented with zinc carbonate and the other was not. Serum zinc concentrations and blood chemistries were sampled on a regular basis. Tissues were taken from dead tamarins for zinc analysis.

The S. mystax is an invaluable laboratory animal model for immunological research. However, in captivity, many of these tamarins are unable to breed and eventually die due to WMS. The fact that S. mystax are zinc deficient may provide an answer to the etiology of WMS.

PHS 6040 (Rev. 1/84)

GPO 904-917

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 00069-02 VR

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Anthropometric Study of the Aotus grisemembra and Aotus trivirgatus

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. M. Renquist	Chief	PU, ACS, VRB, DRS
Others:	D. E. Barnard	Nutritionist Assistant	PU, ACS, VRB, DRS

COOPERATING UNITS *(if any)*
None

LAB/BRANCH
Veterinary Resources Branch

SECTION
Animal Center Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.10	.10	0

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this study is to establish anthropometric parameters for assessing normal growth of Aotus monkeys in captivity, to assess alterations in the development of experimentally treated animals, and to provide an age estimation for primates with unknown birth dates. The anthropometric and dental data collections were made on a regular basis until the animals reached maturity. The anthropometric measurements entailed, head length, head breadth, crown-rump length, foot length, hand length, bitrochanteric diameter and overall length. Thus far it has been determined that weights at six months were between 402 and 563 grams, approximately half that of the adults. Deciduous tooth eruption patterns are similar to other nonhuman primates. It has been observed that the growth rate plateaus at one year and six months of age. The anthropometric measurement correlating most closely with increasing age is the bitrochanteric diameter.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 00070-01 VR

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Development of Mouse and Rat Isozyme Systems Using Isoelectric Focusing

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Kitty P. Smith Genetics Unit CPS, VRB, DRS

COOPERATING UNITS *(if any)*

None

LAB/BRANCH

VRB

SECTION

CPS

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Genetic Monitoring program utilizes several different techniques for protein separation. New techniques are being explored which will make more efficient use of available resources. The isoelectric focusing technique being developed with immobolines in polyacrylamide gels can detect very small differences in proteins which can not be resolved by presently used methods. Seven different genetic phenotypes for Hba have been identified among the inbred strains of mice. Hba can be a very powerful genetic monitoring tool since there are so many genetic differences among these strains.

BEIB Research Projects (Z01 RS)

TABLE OF CONTENTS, (Cont'd)

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10001-16 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pharmacokinetics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Dedrick	Chief, ChES	BEIB, DRS
Others:		
F. Farris	Guest Worker	BEIB, DRS
C. Daniels	Chemical Engineer	BEIB, DRS
R. J. Lutz	Chemical Engineer	BEIB, DRS
F. King	Chemical Engineer	BEIB, DRS
P. F. Morrison	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*
CPB, NCI (J.M. Collins); LMCB-NCI (C.L. Litterst); DR-CC (J.L. Doppman); CP-CC (G. Hook); NTP-NIEHS (H.B. Matthews); SNB-NINCDS (E.H. Oldfield, C. Clark); University of Maryland (M.Egorin; M.F. Flessner).

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.3	1.3	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Pharmacokinetic models are developed for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and man. They provide a plausible set of equations that can be used to extrapolate data from animals to man and thereby improve chemotherapy, and risk assessment. Emphasis has been placed on regional drug administration, and this has led to the devleopment of spatially distributed models of drug transport in tissue. These analyses have provided considerable insight into the penetration depths of drugs administered intraperitoneally or by infusion into the brain. The penetration of cis-dichlorodiammine-platinum (II) (DDP) into peritoneal and subperitoneal tissue is being examined experimentally with an electron probe and the results compared with a reaction-diffusion equation of the process. A lumped model of DDP pharmacokinetics has been developed to include both metabolism to a mobile species and covalent binding to macromolecules. Pharmacokinetic theory which was developed for intra-arterial drug administration combined with hemoperfusion of vascular drainage had been validated experimentally in monkeys. Clinical trials further demonstrated the pharmacokinetic theory. Systemic exposure to BCNU was reduced by 56-87% compared with intra-arterial administration of the same dose. Studies with intracarotid infusion of indocyanine green have demonstrated the ability to remove a large fraction of the infused blood by pumping from the ipsilateral jugular vein.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01-RS-10002-19-BEI

PERIOD COVERED
Oct.1, 1983 to Sept. 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Implant Device Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

John W. Boretos, Physical Scientist, BEIB, DRS

John Doppman, M.D.	Radiologist	CR, CC, NIH
Edward Oldfield, M.D.	Neurosurgeon	NINCDS, NIH
F.T. Hambrecht, M.D.	Health Science Adm.	NINCDS, NIH
William S. Pierce, M.D.	Professor	Penn State Univ.
Murray Eden, Ph.D.	Physical Scientist	BEIB, DRS, NIH

COOPERATING UNITS *(if any)*
CR, CC, NIH; NS, NINCDS, NIH;
FNP, NINCDS, NIH; Penn State Univ., Hershey, PA;
BEIB, DRS, NIH.

LAB/BRANCH
Biomedical Engineering Instrumentation

SECTION
Chemical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, MD. 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.7	0.3

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to elucidate the interaction of biomaterials used for specific implants with the physiological environment and to explore specially prepared biomaterials and design features with respect to their suitability and performance in a variety of contexts. Polyurethanes are an important class of elastomers for use in catheters, heart assist pumps, electrode insulation and similar implant applications. Variations in the basic chemical structure of these polymers as well as physically induced stress can severely reduce their effectiveness for long-term use as a surgical device. Previous studies undertaken by this project have shown a relationship between the molecular chain structure in resisting hydrolytic forces. Recent evidence suggests that physical forces such as stress induced during fabrication can promote a form of stress corrosion. In vitro test data and SEM photomicrographs of surgical explants of various polyurethane classes show that premature failure is often the result of a combination of forces acting on the polymer at stress risers. A strong correlation exists between these in vitro and in vivo observations over short and long term periods of study.

A radiopaque polymer made from a polyol/diisocyanate resin and finely divided tantalum was developed that exhibits good adhesion to polyurthanes and excellent visibility under fluoroscopy. The substance is intended as a marker for catheters and other indwelling devices whose location must be constantly observed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10015-09 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Toposcopic Catheter for Clinical Vascular Use

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: D.R. Shook, Biomedical Engineer, BEIB, DRS
J.L. Doppman, Chief, DRD, CC
E.H. Oldfield Senior, Staff Neurosurgeon. SNB, NINCDS

COOPERATING UNITS *(if any)*
Diagnostic Radiology, CC (A.G. Krudy, N.J. Patronas, D.L. Miller); Surgical Neurology, NINCDS (C. Clark)

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.3	0.5	0.8

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☒ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Toposcopy has been shown to be a reliable, clinical, means to catheterize long, small diameter, and highly tortuous blood vessels, inaccessible by previous techniques. A toposcopic element everts from the tip of a conventional catheter. This extremely flexible polyurethane element has been fabricated in 3, 4 and 5 French sixes mated with 5, 6 and 7 French catheters, respectively, and is capable of eversion lengths in excess of 40 cm.

The toposcopic catheter has been applied clinically for the local delivery of chemotherapy to brain tumors. Treatment is provided by: positioning the conventional catheter in the internal carotid artery from a femoral entry; everting the toposcopic element through the carotid sinus,beyond the ophthalmic artery to avert retinal toxicity; and perfusing the tumor through the middle and/or anterior cerebral arteries. Note that a conventional catheter cannot safely negotiate the tortuosity of the carotid sinus.

The catheter has been extensively used clinically in its present prototype form and production techniques for its fabrication are being transferred to private industry to provide for a ready source of catheters for future studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10018-09 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Particulate Hydrodynamics in Porous Membranes

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.M. Bungay, Chemical Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*
Department of Mathematics, University College, London, England
North Atlantic Treaty Organization, Brussels, Belgium

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Mathematical models are being developed to describe passive membrane transport through pores or intercellular junctions. The Taylor-Aris dispersion analysis is extended to treat combined Brownian motion and convection in a single pore. The solute particle dimension is assumed to be large compared to that of the solvent molecules and also appreciable in size compared to the lateral pore dimension. The latter condition implies strong hindered diffusion and related solute-membrane interaction effects. A key aspect of the analysis is a generalized Einstein relation for predicting axial and radial components of the diffusivity tensor from hydrodynamics solutions for resistance coefficients. Perturbation techniques are used to obtain asymptotic solutions to the hydrodynamic equations, and the method of moments is employed to analyze the solute continuity equation. Related hydrodynamic problems are also being considered, such as flow through constricted vessels.

The hydrodynamic results in combination with an analysis derived from irreversible thermodynamics, provide a predictive theory for simultaneous coupled convective and diffusive transport across porous membranes - either biological or synthetic.

A review of the theoretical approaches to transport in porous membranes is included in the Proceedings of the North Atlantic Treaty Organization Advanced Study Institute on Synthetic Membranes held June 26-July 8, 1983, and directed by the principal investigator.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10034-07 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984.

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Three-Dimensional Histological Reconstruction

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S.B. Leighton, Mechanical Engineer, BEIB, DRS
A.M. Kuzirian, Neuroanatomist, LB, NINCDS

COOPERATING UNITS *(if any)*
LB NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.5	.45	.05

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A semi-automatic system for acquisition of three-dimensional structural information about histological material is being developed. The system should have significant speed and reliability advantages over present techniques using serial sections, although resolution may be limited. In brief, an embedded tissue block will be fixed relative to a scanning electron microscope imaging system, the surface of the block will be imaged and the image stored, and successive slices will be removed by a built-in microtome. Handling and registration of thin sections will thus be eliminated. Human and computer pattern recognition will transform the resulting set of images into a three-dimensional reconstruction. Oxygen plasma etching has been found to give sufficient topographic relief that the resolution of the images is now limited by the SEM and not by the preparation technique. The images of Hermissenda Crassicornis obtained by this technique correlate well with TEM images of the same tissue, indicating that the lack of artifact is adequate for the contemplated studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10039-07 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Biophysical Instrumentation and Methodology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Marc S. Lewis, Research Chemist, BEIB/DRS
Thomas R. Clem, Electronics Engineer, BEIB/DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The project is designed to develop new instrumentation and methodology or improve existing instrumentation and methodology for characterization of biological macromolecules and for studying their interactions. Analytical ultracentrifugation, the techniques ancillary to it, and methods of data analysis using mathematical modeling appropriate for these techniques are the major areas of interest.

Improved precision and optimal efficiency in ultracentrifugal analysis requires improved methods of data acquisition. A microprocessor controlled system for the direct acquisition of data from the photomultiplier tube of the ultraviolet absorption scanner of the ultracentrifuge and for the control of that acquisition has been developed. The software requisite for making this system operational is presently in a developmental stage. When complete, this system will permit direct acquisition of data in digital form while the ultracentrifuge is operating and then permit preliminary data processing followed by transmission of the data to the DEC-10 computer for detailed analysis. This will result in significantly improved precision and enhanced facility in data acquisition and analysis. thus effecting a marked increase in efficiency of research as well as permitting studies where the precision of current methods has not been adequate, such as discriminating between two different models of macromolecular association which have very similar but not identical concentration distributions in the analytical ultracentrifuge.

MLAB, operating on the DEC-10 computer, has been used for mathematical modeling studies for the analysis of various types of protein interactions. These studies have been applied to ultracentrifugal studies of binding and of protein self-association. Such studies are described in the annual report entitled Physical Chemistry of Biological Macromolecules.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10043-07 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Fiber Optic Probes

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

John I. Peterson, Chemist, BEIB/DRS
Randolph E. Patterson H IR CB

COOPERATING UNITS *(if any)*
H IR CB
H IR OD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.8	.8	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A suitable device is needed for the direct measurement of oxygen partial pressure (PO_2) in blood and tissue for both clinical and research applications. Methods currently available for measuring PO_2 lack convenience, reliability, speed, and relevance to many situations of interest. Efforts to develop electrical sensors have not been successful. It is desirable to have a very small PO_2 sensor which can be inserted into a blood vessel of tissue with little disturbance, and which will provide instantaneous and current PO_2 monitoring for either short or extended periods of time. A fiber optic sensor is ideal for this application, with the advantages, for physiological use, of very small size and flexibility, safety, and low cost. A PO_2 sensor has been developed, based upon the principle of fluorescence quenching by oxygen. In the previous year the feasibility of the sensor was demonstrated and its performance evaluated with in vitro and animal tests. Current work is oriented toward converting the sensor to a needle form for experimental use, improving the instrumentation and probe construction, and solving some remaining problems with the sensor system to increase its utility.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10053-06 BEI

PERIOD COVERED
October 1, 1983 to September 30. 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Membrane Based Sampling Systems for In Vivo and In Vitro Kinetic Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.M., Bungay, Chemical Engineer, BEIB,DRS

COOPERATING UNITS *(if any)*
Laboratory of Chemical Pharmacology, DCT

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.1	.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Synthetic membranes are being utilized in kinetics studies to provide a means for continuous sampling of the liquid phases from systems in which a dispersed particulate phase is suspended in the liquid phase. In one application a study of the mammalian blood-brain-barrier permeability is being aided by the development of an apparatus incorporating a sampler in an arteriovenous ex vivo shunt. In this plasmapheresis application, pooling of the plasma filtrate yields a single sample from which the plasma concentration-times-time integral can be evaluated for a chemical administered to the animal. Such sampling systems can be useful for the study of the kinetics of other fluid phase systems for which a membrane can be found that is permeable to one pool of the chemical of interest but impermeable to other pools or another necessary reagent. Thus, other applications might be found in the areas of enzyme kinetics, pharmacokinetics, and the membrane transport of vesicle and cell suspensions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10062-05 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
IEEE-488 General Purpose Interface Bus Program Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.R. Clem, Sr., Electronic Engineer, EEES, BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.2	0.05

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The increased availability and reduced cost of the small desk-top computer has created increased interest in automating data acquisition and process or experiment control in areas where such things were not feasible before due to cost or complexity. With these changes also came a significant increase in the use of the IEEE-488 GPIB by instrument makers. By combining the two, sophisticated instrumentation and data acquisition systems can be assembled quickly and inexpensively. The BEIB is continuing to develop the expertise to provide guidance and assistance to requirements where this approach provides the optimum solution. This capability is further assisted by the BEIB-SERP specifying the IEEE-488 interface on new equipment acquisitions whenever possible. The increase at the NIH, in the numbers and use of the IBM PC has made this capability of great value to the NIH Intramural Research program.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10064-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Indirect Blood Pressure Measurements in Laboratory Animals Using Oscillometry

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

E.C. Walker, Mechanical Engineer, ACES, BEIB

COOPERATING UNITS *(if any)*
SLAMS OD NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.75	0.75	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Presently there are no reliable indirect methods of measuring blood pressure in dogs. Traditional techniques, used in humans, are unsatisfactory primarily because they require the placement of a transducer over the artery being monitored.

Because of the unreliability of traditional techniques we have been investigating a technique called oscillometry. Oscillometry is the method of measuring blood pressure by analyzing the pulse pattern of the cuff pressure oscillations.

In practice, a cuff is placed around a limb and inflated to a pressure above systolic and then slowly deflated. While the cuff is being deflated the amplitude of oscillation in cuff pressure, produced by the arterial pulse beneath the cuff, if monitored. Systolic and diastolic transitions in the oscillometric waveform are then used to indicate the indirect systolic and diastolic pressures respectively.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10065-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 chereacters or less. Title must fit on one line between the borders.)*
Transient Response of Micro-Calorimeter Using R-C Analysis

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS
R.L. Berger, Physicist, LTD, NHLBI

COOPERATING UNITS *(if any)*
LTD, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.20	.20	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In earlier work, we developed an R-C model which enabled us to predict calorimeter performance within 5%. The model revealed several sources of error in the current calorimeter design. With this information, we re-designed the calorimeter to reduce these errors and to offer increased performance and flexibility. The re-design (a) eliminates the air gap, (b) requires only one sensor, (c) can accept all three currently used cell sizes 0.3, 0.5 and 1.0 ml, and (d) increases sensitivity with no significant change in rise-time.

During FY83, this design was implemented and evaluated. All of the above features were realized. However, with the larger cells, the magnitude of the mixing artifact increased to the point that it negated the advantage of using the large cell volume. With the large 1 ml cell, the mixing artifact due to the rotation of the cell averaged 900 micro-joules with a large variability of ± 700 micro-joules.

The major cause of this artifact was found to be a small temperature gradient (4m°C) within the constant temperature chamber. The larger cell volumes were much more sensitive to this gradient than the smaller cells.

The gradient was reduced to less than 0.5m°C by shunting different currents through the heating pads. This reduced the artifact to approximately 100 ±30 micro-joules.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10066-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Egyptian Training Project

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS
H. Metz, Chief, RIS, BEIB, DRS

COOPERATING UNITS *(if any)*
RIS, BEIB, DRS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

As part of a larger project to develop an instrument repair facility in Egypt, a series of lessons in basic electronics was developed. This series was divided into three parts which covered: (1) discrete components (active and passive), (2) digital devices and techniques, and (3) linear devices and techniques. The series consists of 60 lessons with a lab experiment for each lesson. The lessons and experiments were developed in close cooperation with two Egyptian instructors who will be presenting the course in Egypt.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10073-05 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Secondary Emission Mass Spectrometer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

L. Kelner. Visiting Scientists, BEIB

COOPERATING UNITS *(if any)*
LC, NHLBI and LCS, NIMH

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
DRS, National Institutes of Health, Bethesda, MD 20205

INSTITUTE AND LOCATION

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2	1.5	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

During this fiscal year a few modifications have been made in order to improve the performance and versatility of the SEMS instrument. These modifications included: 1) Cs+ ion gun for comparative study of the secondary ion formation under bombardment by particles of different nature; 2) Faraday cup to measure the intensity of primary ion beam more precisely; 3) conversion dinode multiplier and immersion lens to improve secondary ion detection; 4) differential vacuum system for the MS/MS portion of the instrument.

Experimental studies of the particle desorption ionization of labile compounds continued on the instrument, including studies of the primary beam parameters in relation to the resulting mass spectra of the target material. Some of recent biological applications included demonstrating the utility of the SEMS system for biological extract analysis in studies involving the drug induced Parkinsonism in primates and humans.

A new direction in the instrument application has been undertaken this year: an application as a molecular microscope - a device which will detect the spatial distribution of organic substances on the surfaces of biological specimens. The instrument design was presented at the Annual Conference on Mass Spectrometry and Allied Topics on June 1, 1984 in San-Antonio, Texas.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10096-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Light Scattering Method for Evaluation of Platelets

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R. F. Bonner Physicist BEIB DRS

Other Investigators:

T.R. Clem	Elect. Engineer	BEIB DRS
S.B. Leighton	Mech. Engineer	BEIB DRS

COOPERATING UNITS *(if any)*
Bureau of Biologics, FDA
Surgery Br., NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.4	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Assessment of the functional status of platelets for transfusion is confounded by the inherent complexity of the cell, as well as the intricate requirements of sample preparation. A correlation between discoid shape and the functional integrity of the platelet has been established. We have developed a complex automatic machine based on previous experiments with a simple prototype which measures the fraction of the platelets that are discoid and the optical (volume) concentration of unaggregated platelets in standard blood bank platelet concentrate units within their bags. The mircroprocessor-based instrument automatically determines the volume concentration of unaggregated platelets and the fraction that are fully viable (discoid) during a 3-minute measurement sequence following simple insertion of the blood storage bag in the instrument. This process is noninvasive (sterile) and nondestructive. Thus it allows frequent measurements on the platelets prior to transfusion in order to optimize the quality and quantity of transfused platelets given patients. It also allows accurate investigations for optimizing storage and preparation methods. The instrument has been intensively studied with respect to invasive measurements of concentration and morphology of platelets and has proved to be highly accurate. In order to test the clinical significance of these measurements, a clinical protocol has begun in collaboration with Surgery Branch, NHLBI to test the functional qualilty of tested units transfused into patients following cardiac surgery.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10097-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Studies in Cardiovascular Dynamics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.S. Chadwick, Biomedical Engineer, BEIB, DRS
D. McGuire, Mathematician, BEIB
R. Patterson, Chief EPPS, CB, NHLBI

COOPERATING UNITS *(if any)*
NHLBI- Cardiology Branch

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.55	.25	.3

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Theoretical calculations of the contraction of the left ventricle against an arterial system with propagating pulse waves have been undertaken. The dependence of aortic input impedance on frequency, the time course of ventricular and aortic pressure, and ventricular pressure - volume loops are computed using the theory. A model of arteriolar contraction and lumen regulation including the effect of endothelial cells has also been developed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10098-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Laser Instrumentation for Vitreous & Cardiovascular Microsurgery

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
R.F. Bonner Physicist BEIB DRS

P.D. Smith Physicist BEIB, DRS

COOPERATING UNITS *(if any)*
Clinical Branch, NEI
Cardiology Branch & Surgery Branch, NHLBI.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.3	1.3	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study entails the development and methodology of use pulsed carbon dioxide laser systems (one was a prototype pulsed system with fiber optics delivery and the other was a modification of a commercial medical carbon dioxide laser), pulsed Nd:YAG laser coupled to a slit lamp, Q-switched Excimer lasers and high-power CW Argon laser with fiber-optic delivery systems. These laser systems are being tested in a series of animal experiments to test the efficacy and safety of cutting vitreal membranes and of removal of atherosclerotic plaque from the intima of arteries. For the CO_2 and Nd:YAG laser systems systematic studies of animal vitrecomies were performed in order to characterize laser pulse characteristics necessary to transect vitreal membranes. Additional studies of retinal damage as a function of pulse characteristics and distance of cutting site from the retina clarified the potential for use of these laser systems close to the retina. For all laser systems systematic studies of tissue damage on human coronary arteries are in progress to characterize the feasibility (and optimal system design) of laser angioplasty. Evaluation of prototype fiber-optic angioscopes in pigs is being carried out in order to fully explore all facets of technology necessary for clinical laser angioplasty.

Preliminary data reveal that the carbon dioxide laser can cut experimentally created membranes in rabbits for virtually any condition of the clarity of the optical media. The Nd:YAG laser pulses can cut vitreal membranes when power densities exceeding 1 GW/cm^2 are achieved at the target. Moderate to severe turbidity of the optical media greatly decreases the ability to cut vitreal membranes with the Nd:YAG laser and creates the potential for increased retinal damage.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10099-04 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cochlear Mechanics and Hair Cell Transduction

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.S Chadwick, Biomedical Engineer BEIB, DRS
J. Rinzel, Chief MRB, NIADDK
S. Shamma, Staff Fellow, MRB, NIADDK
J. Wilbur, Staff Fellow, MRD, NIADDK

COOPERATING UNITS *(if any)*

NIADDK, Mathematical Research Branch

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.25	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This study is concerned with a theoretical analysis of the propagation of mechanical waves in the cochlea, the traduction process in the cochlear hair cells, and the subsequent propagation of electrical impulses in the auditory nerve. In auditory physiology, both mechanical and neural processes play important roles. This study is intended to clarify their relative roles and interaction.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10103-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Triple Laser-Multi Parameter Flow Cytometry System for Study of Tumor Cell Kinetics

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

W. Schuette, Chief, ACES. BEIB, DRS
S. Shackney NCI
J. Dvorak LPD-NIAD

COOPERATING UNITS *(if any)*
DRS-NCI
LPD-NIAD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3	2	1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A triple laser flow cytometry has been developed so that various immuno-fluorescent labeling techniques may be employed for the investigation of cell kinetics. Three laser beams at different wave lengths are made to intersect a tumor cell flow stream passing through a quartz cuvette so that multi-parameter signals may be obtained. These signals are processed by specialized electronics and then analyzed by means of a PDP 11 computer. Simplified optics have increased light detection efficiency by an order of magnitude. The system is currently being used for the investigation of a unicellular protozon known as trypanosoma cruzi, the causative agent of Chagas disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10109-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Adjunct Heat Treatment of Cancer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.L. Levin, Biomedical Engineer, BEIB, DRS
M. Hagmann, Senior Staff Fellow, BEIB, DRS
J-L Guerquin-Kern, Fogarty Fellow, BEIB, DRS
M. Maxwell, Staff Fellow, BEIB, DRS
A. Zabel, Physician, ROB, NCI
E.J. Glatstein, Chief, ROB, NCI

COOPERATING UNITS *(if any)*
Radiation Oncology Branch, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.0	3.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to facilitate the development of adjunct hyperthermia modalities for cancer treatment by theoretically and experimentally studying the spatial and temporal variation in the temperature field of tissues subjected to microwave and radio-frequency electromagnetic radiation. Currently, we are (1) experimentally measuring the patterns of energy deposition within extremity phantoms produced by various types of helical coil applicators; (2) theoretically describing the electromagnetic interaction of a limb with a helical coil in terms of its design parameters; and (3) theoretically describing the transient thermal profiles within limbs produced by helical coils. We are also performing electromagnetic and thermal modeling of the unwanted non-local energy deposition occuring outside of the hyperthermia applicator.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10110-04 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Dual 3-Dimensional Position Monitor For Speech Analysis: MOD. II

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Neme, title, laboratory, and institute affiliation)*

E.C. Walker, Mechanical Engineer, ACES BEIB

Other Investigators
H.W. Tipton, Mechanical Engineering Tech. ACES BEIB
T.L. Talbot, Mechanical Engineer ACES BEIB
C.L. Ludlow, LCD NINCDS
M. Dorn-Quine, Guest Researcher NINCDS

COOPERATING UNITS *(if any)*
LCD-NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.5	2.0	.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Several speech monitoring instruments have been designed to study the etiology of normal and abnormal articular movements in humans. The first system, which is in current use, provided a unique method of monitoring 3-D lip and jaw movements. The second system, MOD II, an improved version of the first. The device consists of two, mirror image, transducers mounted on a common head frame. Each transducer, which can be individually adjusted, is capable of measuring the movement of a point in three orthogonal planes. The transducers have been structurally and operationally redesigned to provide increased linearity, resolution, and reduced weight. Additionally, the head frame has been totally redesigned to provide improved wearing comfort and reduced weight. The improved system will facilitate studying a broader patient population such as children and the elderly.

Design and fabrication of MOD II has been completed. Results of bench tests indicate that the system performs well, within its specified range. Future efforts will be directed toward patient testing.

Following system entracement, patient testing will be scheduled for the upcoming fiscal year.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10112-04 BEI

PERIOD COVERED: October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*: Analysis of Microcirculatory Blood Flow by Laser Doppler Scattering

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.F. Bonner, Physicist, BEIB, DRS

T.R. Clem, Elect. Engineer, BEIB, DRS

COOPERATING UNITS *(if any)*: Hypertension Br., NHLBI; Lab of Clinical Investigation, NIAID; Lab of Chemical Biology, NIADDK; Allergy and Rheumatogoly Depts., Walter Reed Army Medical Center; MED Pacific, Inc. Seattle, Washington.

LAB/BRANCH: Biomedical Engineering and Instrumentation

SECTION: Electrical and Electronic Engineering

INSTITUTE AND LOCATION: National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.4	1.4	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is the development of a clinical, non-invasive monitor of tissue blood flow by analysis of the spectrum of Doppler-scattered laser light. The NIH Laser Doppler Blood Flow Monitor has been demonstrated to be highly portable and clinically convenient with sterilizable, rugged flexible 4m fiber optic probes and portable photodiode detection system. The linearity of the flow analysis processor has been demonstrated in a variety of tissues and clearly resolves physiologic flow changes including pulsatile flow in the microcirculation. Muscle blood flow in over 50 patients with neuromuscular disease has been studied and data suggest that post occlusive reactive hyperemia responses may be primary or secondary indicators of disease state. Measurements of local muscle blood flow dynamics in patients with neuromuscular diseases indicate abnormalities distinct to different disease types. Nasal blood flow has been shown to be a quantitative measure of the physiologic response of the nose to drug challenges. Scleroderma patients' fingertip blood flow appears to fall in three easily-discernable classes associated with the severity of the disease and a simple measurement protocol may elucidate efficacy of drug therapy. Studies show a characteristic local oscillatory flow pattern in a capillary microcirculation of the skin in sickle cell patients which appears to correlate with severity of disease and its response to drug therapy. Similar oscillations presumably due to myogenic arterioler smooth muscle vasomotion are characteristic of several hypertensive patients, particularly those on durgs inducing peripheral vasocontriction. Preliminary studies on patients with Type I diabetes have shown abnormalities potentially related to the etiology of the microvascular component of long-term type I diabetes. In summary numerousongoing clinical studies seek to characterize microvascular functional abnormalities and their role in a number of diseases with microvascular components.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10114-03 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Phasic Aortic Pressure Control System for Awake Dogs

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S.R. Goldstein, Chief, MES, BEIB, DRS
M. Maxwell, Staff Fellow, BEIB, DRS,
R. Patterson, Chief, EPPS, CB, NHLBI

COOPERATING UNITS *(if any)*
CB, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.75	.65	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A system for manipulating phasic aortic blood pressure in closed chest experimental dogs has been under development. An intra-aortic balloon residing in the descending aorta and controlled by feedback from a catheter tip pressure tranducer is phasically inflated or deflated by a piston type actuator to vary the pressure to conform with a predetermined desired pressure waveform. While still under servo control, the balloon is reset (either filled or deflated) every few beats due to the action of a roller pump which bypasses the systemic circulation in order to withdraw (or infuse) blood into the aorta. In this way it was hoped to control both the average pressure level and the exact waveform so that the effects on the myocardium of various drug interventions could be evaluated independent of their effects on systemic blood pressure.

During the past year the system was evaluated both in dogs, and in an elaborate in vitro model of the aorta and systemic circulation. A number of problems were identified which could only be solved by placing constraints on the system which ultimately proved to be mutually incompatible -resulting in termination of the overall effort. The fundamental problem which could not be overcome arose from the large phase shift and lack of attenuation with increasing frequency between actuator position and aortic pressure which arises due to the distributed compliance and low wave speed of the aorta. This undesirable open loop characteristic precluded attempts to design suitable servo compensation, resulting in phasic waveforms that did not faithfully reproduce the desired waveform. This situation could be partially mitigated only by making the balloon small- which resulted in a need to reset the balloon too often for the system to function properly.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10116-03 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Modeling of Arterial Pulse Waves

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.S. Chadwick,	Biomedical Engineer,	BEIB,DRS
D. McGuire,	Mathematician,	BEIB
D. Goldstein ,	Senior Investigator	EHL, NHLBI
H. Kaiser,	Chief EHL,	NHLBI

COOPERATING UNITS *(if any)*
NHLBI, Endocrine-Hypertension Laboratory

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.55	.25	.3

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A new theory was developed to compute the propagation of the pressure wave in a branching system. The theory includes cross sectional area and stiffness variation, viscous and viscoelastic effects, and side branch flow. The theory was then used in an analytical model of the brachial artery system which can reproduce the phasic pressure waveforms as measured in normal and hypertensive subjects. Particular emphasis was directed toward an understanding of the genesis of the peripheral dicrotic wave, and its modulation by vasoactive drugs.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10122-03 BEI

PERIOD COVERED: October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*: Micro-computer Controlled Fermentation System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.R. Clem, Sr., Electronic Engineer, EEES, BEIB, DRS

Other Investigators:

Y. Shiloach	Chief, Pilot Plant	LCDB NIADDK
A. LeRoy	Chemical Engineer	BEIB, DRS

COOPERATING UNITS *(if any)*: LCDB - NIADDK

LAB/BRANCH: Biomedical Engineering and Instrumentation Branch

SECTION: Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION: DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.5	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A process control system using a small desktop computer as the central control element is continuing to be developed for the NIH Fermentation Pilot Plant. The various monitoring transducers and controlled elements (pumps, valves, etc.) are connected to the computer via the IEEE-488 General Purpose Interface (GPIB). For maximum versatility most components used are commercially available items (instruments, meters, etc.). The GPIB-based design allows changes in the parameters measured or controlled, or scaling to different size vessels to be accomplished relatively quickly and easily. Some instruments, though, are connected to the controller through direct hardware I/O connections. Utilizing the computational capabilities of the computer/controller allows initial selection of the operating parameters and dynamic alteration of these parameters as the process continues, thus allowing optimization of yields or detailed study of the process parameters.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10126-03 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*
Trace Analysis and Elemental Microanalysis in Biological Materials

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

A.F. LeRoy, Chief, Analytical Methods Sect., BEIB, DRS
M. Linnoila M.D., Ph.D., CPB, NIMH
S. Tsai, Ph.D., LCM, NHLBI
P. Galle, Prof. of Biophysics. Medical Faculty, Creteil, France
G. Mathe, Director, ICIG, Villejuif, France
B. Hecquet, Ph.D., Centre Oscar Lambret, Lille, France
P. Parsons, Ph.D., BEIB, DRS

COOPERATING UNITS *(if any)*
CPB-NIMH; LCM-NHLBI; LCP-NIAMDD, LMP-NCI; ICIG-Villejuif, France;
Biophysics Department, Medical Faculty-Creteil, France;
Centre Anticancereux "Oscar Lambret", Lille, France

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Analytical Methods

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.75	1.25	.50

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Atomic absorption spectrophotometry using electrothermal atomization and neutron activation analysis have been used for the quantitation of platinum, vanadium, nickel, cobalt, calcium, and iron and some other elements in biological tissues and fluids. Electrochemical techniques are being developed for analysis of some elements. The analyses are important in clinical biochemical, pharmacokinetic and binding studies. The analytical techniques must be very sensitive because in most instances these elements are present in trace concentrations in the samples typically of interest e.g. part-per-million (10^{-6}g/g), part-per-billion (10^{-9}g/g), and in some cases even the part-per-trillion (10^{-12}g/g) while sample volume is also often small (typically 0.5 ml or less). Various separation techniques such as chromatography, solvent extraction, and electrophoresis have been used to purify samples and fractionate and concentrate chemical species for analysis and reduce or eliminate interferences.

Microprobe techniques using instruments such as the electron probe microanalyzer have also been used to localize elements on the microscopic scale in sub-cellular structures in different tissues.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10132-03 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less Title must fit on one line between the borders.)*

Image Processing and Cell Classification

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J. R. Ellis, Expert, BEIB/DRS

Other Personnel
C. C. Gibson Electronics Engineer BEIB/DRS
M. A. Greenwood SNB/NINCDS
J. Edwards SNB/NINCDS
T. Baginski SNB/NINCDS

COOPERATING UNITS *(if any)*

SNB/NINCDS

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.45	0.25	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In vitro cell culture is an effective method for the study of the effects of chemotherapeutic agents on neurological tumors. Quantitation of all but the most rudimentary of these effects is generally beyond the ability of human observers. Thus, an automated system for acquisition of image data, extraction of parameters of interest, and statistical processing of results is necessary for any quantitative effectiveness.

Historically, this field has been qualitative. Thus, moving toward quantitative evaluations has involved a very broad spectrum of discussions about methods, limitations of methods, desired results, and significance of results. Specifically, it is necessary to prepare cultures and micrographs differently for human visual inspection and for reliable machine processing. In addition, it has been necessary to clarify the strong and weak points of human and automated image processing.

This has been especially important in this project because the system originally purchased was ill-suited to the tasks envisioned and support from the manufacturer was totally inadequate. Thanks largely to the efforts of C. C. Gibson of BEIB, the system has been substantially rebuilt and made much more reliable and capable. As a result, in vitro cytotoxicity assays of the effects of AZQ, BCNU, and other drugs on Glioma tumor cell lines using cell counts over titer plates have become a reliable production operation.

Morphology studies using size, aspect ratio, and a shape factor were begun on micrographs of granules and mitochondria. These studies could be continued in the future. However, the laboratory has been reorganized following certain personnel changes. As a result, studies other than cell counting are allowed to the extent that they do not interfere with this production operation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10135-03 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

The Effects of Fluid Shear on Cultured Endothelial Cells

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.J. Lutz Chemical Engineer, BEIB/DRS

P.M. Bungay Chemical Engineer, BEIB/DRS

COOPERATING UNITS *(if any)*

American Red Cross
FDA

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Chemical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD. 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Many pathophysiological processes in the cardiovascular system such as thrombosis, vessel wall injury, and atherosclerosis occur in the presence of fluid shear forces. These shear forces have a direct mechanical effect on the vessel wall and can also indirectly affect wall properties by mediating the interactions of blood elements with the lumenal surface. The normal integrity of a vessel wall is maintained by a delicate monolayer of endothelial cells grown in monolayer culture. Morphological, cytoskeletal, and metabolic changes in the endothelial cells are being investigated as a function of fluid shear stresses on the cell surface. A parallel plate flow chamber was specially designed to accommodate Thermanox circular cover slips upon which human umbilical cord endothelial cells are cultured. The flow patterns and shear stress values within the chamber have been characterized using electrochemical shear measurements, flow visualization techniques, and laser doppler anemometry during steady flow. We have tested the chamber at shear stresses up to 20 dynes/cm^2. The rate of development of cell orientation in the monolayer was observed as a function of shear stress from no flow to 16 dynes/cm^2. Radio-immunoassays were developed to measure levels of von Willibrand factor, Factor VIII:R, and prostacyclin in the culture medium associated with release/production by the endothelial cells. The utility of these assays to follow the appearance of the substances as functions of time and shear stress intensity will be improved by increasing the proportion of monolayer area to culture medium volume. Alternatives to the parallel plate flow chamber with higher area-to-volume ratios were examined. A cup-and-bob viscometric system was chosen for more detailed evaluation. One option being explored is to use the viscometer to shear suspensions of cross-linked dextran microcarrier beads coated with the endothelial cell monolayers.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10136-03 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Imaging in Positron-Emission Tomography

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J. R. Ellis Expert BEIB/DRS

Other Personnel:
R. M. Kessler NM/CC
M. Eden Chief BEIB/DRS

COOPERATING UNITS *(if any)*
NM/CC

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Office of the Chief

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.25	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Positron-Emission Tomography (PET) and emission computed axial tomography (ECAT) offer unprecedented opportunities to visualize and measure in-vivo organ metabolism. Our current interest centers on the brain, perhaps the least accessible region of the body to non-invasive diagnostic probes.

One desirable goal of image processing in this field of interest is determination of volumetric metabolic activity from collections of scan plane data. Our work on data spreading and attenuation due to finite object size (partial voluming) has made specification of object recovery as a function of system resolution possible. Thus, axial sampling can be chosen to maintain visibility of, or activity recovery from, objects of a selected minimum size through a set of scan planes.

With such choices. it is possible to relate scan plane data to a three dimensional model of the brain robustly. Use of such a model can allow meaningful comparisons of data taken from subjects with different orientations and locations relative to the PET or ECAT frame of reference.

Another, more ambitious, goal is to make a dynamic model of brain activity. Then, one can use time-series PET or ECAT data to estimate biological quantities in functional compartments. Further analysis allows estimates of the parameters of the kinetic rate equations relating them.

Work has been underway on these topics.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10137-03 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*

Processing of Electron Microscope Images

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

J. R. Ellis, Expert, BEIB/DRS
T.G. Pun, Visiting Fellow, BEIB/DRS
C.E. Fiori, Physical Scientist BEIB/DRS
R.D. Leapman, Visiting Scientist. BEIB/DRS
C.R. Swyt, Physicist. BEIB/DRS
G. Hook, Staff Fellow, BEIB/DRS

COOPERATING UNITS *(if any)*

CSL/DCRT

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An overall goal of the DRS-BEIB/DCRT-CSL Electron Beam Imaging and Microspectroscopy (EBIM) Project is to obtain chemical elemental maps of biological samples with resolution in the sub-micron range which are subjectively satisfying and objectively meaningful. Our image processing work associated with this project has developed with essentially four foci consistent with this broad target area: 1) Quality enhancement, 2) pixel value and uncertainty estimation for normalized functions of the raw data, 3) controlled parameter image generation, and 4) provision of a sufficiently friendly user interface for a user to employ tools developed to satisfy the first three points.

Our definition of quality enhancement for a set of images with dissimilar characteristics includes making them compatible for comparison using overlays and other forms of composition by expansion, contraction and smoothing. It also involves construction of collages or montages from several images, background subtraction, region edge enhancement, and matching of desired signal ranges to the eye's response.

Significant new analytical and simulation results have been obtained concerning the statistical variations to be expected for EEL elemental edges and X-Ray elemental peak-to-background ratios. Work on improved pixel and region value estimation for normalized functions is in progress.

Synthetic images with controlled parameters can be used very effectively in resolving questions of object visibility and artifact generation in this project.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10143-03 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Interaction of Body Temperature and Sleep Rhythms

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

T.L. Talbot, ACES, BEIB, DRS
Wallace Mendelson, Psychobiology, NIMH
M. MacCollum ACES, BEIB, DRS

COOPERATING UNITS *(if any)*

Psychobiology Lab-NIMH

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.7	1.2	0.5

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Clinical evidence suggests a correlation between core body temperature and the frequency of sleep episodes. An artificial thermoregulatory system is completed which will enable core body temperature manipulation. This device permits the evaluation of the efficacy of thermal regulation in the treatment of sleep disorders. Clinical trials are now performed on a regular basis. Simultaneous sleep recordings are obtained during both a non-manipulated and manipulated 24 hour period.

Clinical studies are now underway and the data obtained so far suggests no interaction between sleep rhythms and body temperature. More studies are being performed to substantiate conclusively these findings.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10146-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Prosthetic Urethral Sphincter

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

S. B. Leighton, Mechanical Engineer, BEIB, DRS,
Marston Linehan, M.D., DCT, NCI
Stevenen Scoog, M.D. WRAMC

COOPERATING UNITS *(if any)*
DCT, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.1	.1	0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A number of techniques are used for treating urinary incontinence, including a number of artificial prosthetic sphincters. The present work concerns an entirely intraurethral artificial sphincter that can be implanted without surgery. Concepts are being explored which would allow the device to be used in situations in which surgery is contraindicated, and would also presumeably lower the cost. The valve would be appropriately matched to urethral dimensions, pressures, and flowrates. The valve would be potentially useful in cases of nonopening normal valves as well as in cases of non-closing valves.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10147-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Viscoelastic Properties of the Erythrocyte Membrane

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Aydin Tozeren, Visiting Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
Bioengineering Institute, Columbia University, N.Y.
Shu Chien, M.D., Ph.D.
Richard Skalak, Ph.D., K.L.P. Sung, Ph.D.

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.30	0.30	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The erythrocyte membrane is modelled as a two dimensional viscoelastic continuum that evolves under the application of stress. The present analysis on the erythrocyte membrane is motivated by the recent development of knowledge on its molecular structure and by its complex behavior exhibited in dynamic micropipette testing and in tank treading during shear flow. The proposed constitutive equations have the form similar to that of a two dimensional Kelvin model with a constant area condition. However, the membrane viscosity is made to depend on the rate of strain and the elastic strain tensor is measured from the evolving preferred configuration.

The constitutive equations proposed in the present analysis explain in a consistent manner the data on both the deformation and recovery phases of the micropipette experiment. The rheological equations of the present study are applied in a later section to the analysis of a plane membrane deformation that is quantitatively similar to the tank-treading motion of the erythrocytes in a shear field. The computations yield useful information on how the membrane viscosity becomes a more dominant feature in tank-treading motion. The present model reflects the microstructure of the erythrocyte membrane. A membrane composed of a lipid bilayer may be idealized as a viscous membrane with a constant area condition. The network of protein molecules embedded in and attached to the lipid bilayer of the erythrocyte membrane serves as a storage medium for the elastic strain in the membrane. The molecular organization of this network evolves continuously during a prolonged deformation. The material constants appearing in the proposed constitutive equations may be useful indicators of the biochemical state of the membrane in health and disease.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10148-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Analysis of the Coupling Between Left Ventricle and Vascular System

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, end institute affiliation)*

Aydin Tozeren, Visiting Scientist, BEIB, DRS

COOPERATING UNITS *(if any)*
Dr. Shu Chien, Department of Physiology, Columbia University, New York

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.30	0.30	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The aim of this study is to develop equations governing left ventricular pressure and volume during a cardiac cycle. It is assumed that the stress in the myocardium is composed of an isotropic tissue pressure term and fiber tension. Fiber tension T depends on the stretching and rate of stretching of cardiac fibers as well as an internal variable c that describes the degree of electrochemical activation of the muscle fiber. Using mechancial equations of equilibrium and the constitutive equations mentioned above, a time dependent pressure-volume relation (P-V) is obtained for the left ventricle. Hydraulic characteristics of the large arteries are modelled by a three parameter windkessel model. It is assumed that the aortic pressure is equal to the ventricular pressure P when the aortic valve is open. Mechanical events of the cardiac cycle are considered as a function of heart rate by changing one of the following parameters: end diastolic volume EDV, contractility c_o, time constant of contraction w, and resistance R and compliance C of the large arteries. For given EDV, an increase in HR leads to increases of both systolic pressure P_s and diastolic pressure P_d with a decrease of pulse pressure, and a decrease of ejection fraction, and a biphasic change in cardiac output CO, which increases at first to reach a maximum and then decreases. When w is doubled, the rate of pressure rise and maximum flow rate are approximately doubled, but there is very little change in stroke volume SV, P_s and P_d for moderate HR. At higher HR levels, cardiac output CO increases with w because of the lengthening of diastolic phase; aortic valve opens at an earlier time. An increase in c_o increases CO as well as P_s and P_d, regardless of HR level. SV and CO vary inversely with R and directly with the slope of the isovolumetric P-V curve.

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NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10149-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Constitutive Equations of Skeletal Muscle Based on Cross-Bridge Mechanism

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigetor.) (Name, title, laboratory, and institute affiliation)*

Aydin Tozeren, Visiting Scientist, BEIB
Mark Shoenberg, Senior Investigator, LPB, NIAID
Evan Eisenberg, Section Chief, IRLC, NHLBI

COOPERATING UNITS *(if any)*
LPB, NIAID
IRLC. NHLBI

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Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.40	0.40	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Statistical mechanics of cross-bridge action are considered in order to develop constitutive equations that express fiber tension as a function of degree of activation and time history of speed of contraction. The kinetic equation of A.F. Huxley (Prog. Biophys. Mol. biol. 7:255,1957) is generalized to apply to the partially activated state. The rate parameters of attachment and detachment and cross-bridge compliance are assumed to be step functions of extension, x, with a finite number of discontinuities. This assumption enables integration of the kinetic equation and its moments with respect to x analytically resulting in equations where x has been eliminated. When the constants in the rate parameters and the force function are chosen such that Hill's force-velocity relation and features of the transient kinetic and tension data can be fitted, the resulting cross-bridge mechanism is quite similar to the one proposed by Podolsky and co-workers (Proc. Natl. Acad. Sci. USA, 64:504, 1969). Because the derived constitutive equations simplify mathematical analysis, they enable the evaluation of the influence of various cross-bridge parameters on the mechanical behavior of muscle fibers. For example, (ix) Instantaneous elastic response (T_0 - T_1) and the magnitude of rapid recovery (T_2 - T_1) after a step length change can be explained well when the rate of attachment is assumed high for positive x. In that case T_2 corresponds to the force generated by cross-bridges in the region of negative x; (ii) Kinetic transients occur as a result of the jumps that exist in the distribution of attached cross-bridges during the isometric state. Because of the hyperbolic nature of the kinetic equation, these jumps propagate in the -x direction causing rapid changes in the speed of contraction. This study is further extended to take into account of multiple action sites and cross-bridge interaction. In the simplest case (transient response after a step length change) the model reduces to set of 14 ordinary differential equations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10151-02 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less Title must fit on one line between the borders.)*

Nuclear Magnetic Resonance Imaging

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Dr. David I. Hoult, Physical Scientist, BEIB, DRS

Other personnel:
Dr. Ching-Nien Chen, Expert
Dr. Victor J. Sank, Expert
Dr. L. Kyle Hedges, Staff fellow
Mr. Michael S. Silver, Student

COOPERATING UNITS *(if any)*

Department of Radiology, Clinical Center

LAB/BRANCH

NMR Imaging Laboratory, Biomedical Engineering and Instrumentation

SECTION

Office of the Chief

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.2	3.8	0.4

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

In the past year, effort in nuclear magnetic resonance imaging has been expanded on several research fronts.

A. Following the failure of the magnet manufacturer to install successfully the clinical NMR imaging system in the Department of Radiology. Clinical Center, the research group took over the homogenizing of the magnetic field necessary for clinical imaging, and, using a new technique, achieved the specified homogeneity, thereby enabling the Radiology department to produce high quality images.

B. Considerable controversy exists within the NMR image community over the choice of an optimal field strength for imaging. Bench methods were developed for accurately assessing the signal-to-noise ratio from, and radio-frequency power deposition in, the human body at any frequency used for imaging. It is hoped these results will help resolve the matter.

C. A pulse for highly selective spin population inversion has been discovered. The result is of considerable experimental and theoretical importance for it represents only the second known analytical solution of the non-linear differential equations governing the motion of an NMR spin system. Further, above a critical threshold, the inversion is independent of applied power.

D. A so-called "quadrature" probe system has been invented which reduced radio-frequency power dissipation in the body by almost a factor of 2 while improving signal-to-noise ratio by almost 40%.

E. The electronic upper frequency limit for adult head imaging has been pushed from 84 MHz to 130 MHz with the aid of a novel phased-array receiving coil.

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NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10153-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
A Position Sensor for Computer Modeling

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

H. E. Cascio, Electronic Engineer, BEIB, DRS
P. Smith, Visiting Scientist, BEIB, DRS
S. Leighton, Mechanical Engineer, BEIB, DRS
R. Feldmann, CCB DCRT

COOPERATING UNITS *(if any)*
CCB, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.45	0.15	0.30

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For the study of macromolecular structure and of molecular interactions. the use of a computer generated display of the molecule is a powerful interpretive tool. In particular, the ability to be able to manipulate in space, i.e. to rotate and translate the molecule(s) to any desired orientation enhances the usefulness of the device. A further degree of sophistication is to provide a feedback mechanism giving an indication of the repulsive or attractive forces (Van der Waals interactions) present as two molecules are fitted together or as a single molecule is twisted to a new conformation. A joy stick apparatus has been designed to provide these features. Two molecules or part of the same molecule can then be rotated and translated in any direction. With each new position, the computer program re-evaluates (on a one millisecond timescale) the appropriate forces to provide the investigator with a feel of the total forces involved.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10155-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Vidicon Detection for Fluorescence Microscopy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

H.E. Cascio, Electronic Engineer, BEIB, DRS
P. Smith, Visiting Scientist, BEIB, DRS
R. Balaban, Staff Fellow, KE NHLBI

COOPERATING UNITS *(if any)*
KE, NHLBI

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Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.1	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

For one dimensional spectral analysis of the fluroescent properties of kidney microtubules, a vidicon detector has been mounted at the image plane of a microscope. The Princeton Applied Research model 1216/1254 detector is ideally suited for this application in that the scanning parameters of the vidicon are readily adjustable to provide the optimum configuration for the viewed image. However, for initial sample set up, and for two dimensional data collection, the lack of a standard video mode is a limitation. A modification has been made to this detector to produce an optional standard composite video signal. The existing preamplifier in the model 1254 detector is a charge sensitive preamplifier which integrates the video signal across each horizontal scan line. This integration causes a loss of resolution in the horizontal direction, when used in the standard video mode. A fast video preamplifier was designed and placed inside the preamplifier housing with the original preamplifier. A command from the computer terminal selects the scanning mode and connects the proper preamplifier into the system.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10156-02 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less Title must fit on one line between the borders.)*

Differential Scanning Calorimeter

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Neme, title, leboratory, end institute affiliation)*

C.P. Mudd, Biomedical Engineer, ACES, BEIB, DRS
T. Talbot, Mechanical Engineer, ACES, BEIB, DRS
R.L. Berger, Physicist, LTD, NHLBI
P.D. Ross, Physical Chemist A LMB, NIADDKD

COOPERATING UNITS *(if any)*

LTD, NHLBI
A LMB, NIADDKD

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The transfer of sensor design and modelling techniques to the field of differential scanning calorimetry from earlier work in differential heat conduction calorimeter has resulted in two models of differential scanning calorimeters which should satisfy the sensitivity and scan rate requirements. One system uses two sensors and takes the difference electronically while the other system used only one sensor which operates as a null detector in two match thermal channels.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10157-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Temperature Controlled Chamber for X-ray Diffraction Specimens

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd Biomedical Engineer, ACES, BEIB,DRS
H.W. Tipton Mechanical Engineering Tech. ACES, BEIB, DRS
A.V. Parsigian, Research CR,PSL
B.K. Lee, Researcher CR,PSL

COOPERATING UNITS *(if any)*
DCRT, CR-PSL

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER
0.1	0.1	

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A proto-type chamber was constructed of lexan with a 1 cm diameter beryllium window to allow the x-ray beam to enter the chamber. The specimen is mounted in a holder next to the beryllium window. The edge of the holder is mounted to the lexan case to preserve the vacuum seal while the center area of the holder is mounted to a Peltier solid state heat pump. The other side of the heat pump is connected to a heat sink. A thermistor mounted next to the specimen in the holder controls the heat pump to keep the specimen at the set temperature. The film plate is mounted inside the chamber on an adjustable bracket. The chamber will hold a vacuum of 0.01 atm while the controller keeps the specimen at any temperature between 4°C and 70°C with a stability of + 0.2°C.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10158-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Isolated Heart Perfusion

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

M.A. MacCollum, Mechanical Engineer, ACES, BEIB, DRS,
Greg Ribakove, M.D. Heart Surgery, NHLBI

COOPERATING UNITS *(if any)*
Surgery Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.2	.1	1.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

An apparatus for perfusion of isolated rat hearts has been developed which circulates a buffered blood analog. This device is used to investigate biochemical and physiological parameters of the heart. including blood pressure, pulse pressure, cardiac output, tissue pH and others. The system allows investigators to induce temporary cardioplegia, during which pharamacologic agents may be introduced into the modes of operation: working heart, ischemia (both warm and cold) and Langendorf aortic perfusion. Comparing the pre- and post-plegic parameters allow the investigators to assess the ability of certain drugs and procedures to sustain cellular life through ischemic periods.

The results gained from the isolated heart experiments will be tested in large animals in vivo, using the same parameters along with animal survival after surgery.

Engineering refinements in the perfusion circuit described above are completed and the system is fully operational.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10159-03 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Pathophysiology of Cachexia in Sarcoma Patients

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
R.Corsey Electronic Engineer BEIB, DRS

Others:
J.A. Norton Section Chief SURG,NCI
J.F. Moley Research Associate SURG, NCI

COOPERATING UNITS *(if any)*
Anesthesiology Service, Clinical Center, NIH (D.E. Lees)
Nutrition Department, Clinical Center, NIH

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Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	1.5	0.5

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The first phase of this study has demonstrated that patients with metastatic disease have higher levels of energy expenditure than controls, and patients with extremity sarcomas have slightly higher levels of energy expenditure than controls. The next phase will determine if glucose oxidation, whole body protein turnover and potassium 40 levels are different in preoperative sarcoma patients from controls. Sarcomas are useful for understanding the pathophysiology of cachexia in that they usually do not alter the patient's ability to aliment himself, they are metabolically active and patients bearing them have been shown to have an increase in glucose consumption across tumor - bearing limbs. Stable isotopes in the forms of 13C-glucose and 15N-glycine and 13C-leucine are not radioactive and are very safe to administer. The study will determine if any difference demonstrated by measurements of isotopes can be correlated with tumor size or growth.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10162-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Wound Healing: Biology and Rheology

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Thomas L. Talbot, MS, ACES, BEIB
Walter T. Lawrence M.D., C. Surgery, NCI
Lawrence E. Thibault, ScD. Bioengineering Dept, Univ. of Pa

COOPERATING UNITS *(if any)*
DRS, NCI, University of Pa, Philadelphia, Pa

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Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.2	1	0.2

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Preliminary studies have been completed with swine models. These studies involved stamping an indelible gird (10cmx10cm) on the skin of the swine, and the excision of a 1 cm by 10 cm strip of the skin out of the grid area, and finally approximating the incision edges with silk sutures. Photographs of the grid were taken before excision, after excision, and after suturing. These photographs will be analyzed to determine the impressed strain on the wound closure and eventually relate this information to wound breaking strength (WBS).

Studies have been completed using a rat model which relate biologic and pharmocologic interventions to WBS. Certain groups were pharmacologically intervened during the wound healing process. Significant decrease in WBS was observed in these groups as compared to control groups. Further studies will include the comparison of tumor bearing group to control groups.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10163-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Magnetoencephalographic Localization of Foci of Neurologic Activity

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.D. Smith	Visiting Scientist	BEIB, DRS
R.F. Bonner	Physicist	BEIB, DRS
W.S. Friauf	Section Chief	BEIB, DRS
S. Sato	Sr. Investigator	EB NINCDS
R. Porter	Chief	EB NINCDS
M. Nisenoff	Chief	NRL

COOPERATING UNITS *(if any)*
Epilepsy Branch, NINCDS; Naval Research Laboratory

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.8	0.2

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A continued collaboration with the Naval Research Laboratories has enabled a SQUID magnetometer to be used to study inter-ictal spike discharges in epileptic patients. Correlation of the MEG activity and the corresponding EEG signal for these discharges permits signal averaging of spikes associated with the same neurological event. These measurements allow a magnetic field map at the surface of the scalp to be obtained from which a prediction of the source of the epileptic focus can be made. Computer and electronic processing techniques have been developed to analyze these MEG and EEG signals with the aim of producing an efficient method of localizing the sources of the epileptic discharges in a selective manner. Several patients have been scanned using these techniques. To enhance the collection of MEG data associated with a single spike discharge, a seven channel array detector has been specified.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10170-02 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Biological Applications of a Computer Controlled Analytical Electron Microscope

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Visiting Scientist	BEIB, DRS
Others:		
C.E. Fiori	Physical Scientist	BEIB, DRS
C.R. Swyt	Physical Scientist	BEIB, DRS
K.E. Gorlen	Electronic Engineer	CSL, DCRT
C.C. Gibson	Electronic Engineer	BEIB, DCRT
R.L. Ornberg	Senior Staff Fellow	LCBG, NIADDK

COOPERATING UNITS *(if any)*
DCRT, NIADDK

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.5	2.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The computer controlled analytical electron microscope developed jointly by BEIB and CSL, DCRT, provides a unique tool for measuring sub-cellular elemental distributions with a resolution of some 10 nm. Experiments have been carried out to test the capabilities of the instrumentation and to develop further the methodologies for analysis. Nitrogen electron energy loss images have been recorded from cryofixed pancreas beta and adrenol chromaffin cells. Calcium and nitrogen maps have been obtained from rapidly frozen and freeze substituted spinal cord neurons, treated with potassium and sodium glutamate to produce calcium deposits in their mitochrondria. In these images it has been found crucial to model the spectral background correctly and a one-parameter fit, which is often assumed, in general leads to artifacts despite an apparent improvement in signal-to-noise ratio. Ratio maps of nitrogen to phosphorus or sulphur can be obtained from the appropriate x-ray images and these ratios can be related to the biochemical constituents of organelles. New software controlling the DeAnza image display system allows quantitation of the chemical maps. Thus, for example, the ratio image of two energy loss maps eliminates, to first order, the effects of plural scattering. It has been possible to quantitate x-ray microanalysis in thin cryosections by using inelastic electron scattering as measured by EELS to determine the mass per unit area in 100 nm diameter regions at extremely low dose (approximately 100 electrons nm^{-2}). This enables quantitative measurements to be made from hydrated cryosections, including an estimate of the water content. Forthcoming improvements in the electron energy loss spectrometer should provide increased sensitivity and allow annular dark field STEM imaging to be carried out simultaneously. It will also be possible to perform Z-contrast imaging in suitably thin samples. This new contrast mode is predicted to depend only on local mean atomic number and thickness effects are cancelled.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10182-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*
Study of Cartilage Mineralization by Analytical Electron Microscopy

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman	Visiting Scientist	BEIB, DRS
E. Livne	Visiting Scientist	LOBP, NIDR
C.E. Fiori	Physical Scientist	BEIB, DRS
C. Oliver	Biologist	LOBP, NIDR

COOPERATING UNITS *(if any)*
LOBP, NIDR

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The distribution of calcium in mouse mandibular condyle was investigated by electron energy loss spectroscopy in order to determine the role of the matrix vesicles in cartilage mineralization. Ultrathin embedded cartilage sections from 1 week, 1 month, and 1 year old animals were analyzed both at the surface of the condyle and at different depths. High calcium concentrations were found inside vesicles near the mineralization but matrix vesicles close to the surface did not contain appreciable amounts of calcium either crystalline or amorphous. This suggests that the matrix vesicles near the surface may be involved in other processes, such as the fibrillation which occurs in non-inflamatory ulceration of cartilage or osteoarthritis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10183-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Elemental Imaging of Nerve Terminals and Cerebellum

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.D. Leapman Visiting Scientist BEIB DRS

Others:

S.B. Andrews	Special Expert	LN, NINCDS
T.S. Reese	Chief	LN, NINCDS
C.E. Fiori	Physical Scientist	BEIB, DRS
C.R. Swyt	Physical Scientist	BEIB, DRS

COOPERATING UNITS *(if any)*
Computer Systems Laboratory, Division of Research and Technology, NIH (K.E. Gorlen), LN/NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Distributions of potassium, sodium, calcium, phosphorus and sulphur were obtained from dried cryosections of rapidly frozen synaptosomes and cerebellum. The synaptosomes derived from cholinergic endings of squid optic lobe were imaged by emission of characteristic x-rays with the use of an energy dispersive spectrometer. Specimens were cooled to -120°C in a special cryotransfer sample stage, in order to minimize mass loss by radiation damage. The digitally acquired elemental maps showed a bimodal distribution of potassium and sulphur in the synaptosome population. This result suggests that only a fraction of synaptosomes with high potassium and low sodium are physiologically equivalent to the cholinergic endings of in vivo cells.

In an effort to understand changes in potassium and calcium concentrations that occur in cerebellum trauma, rat cerebellum cryosections were analyzed. Although little contrast, apart from compression artifacts , was visible in the elastic images, potassium maps obtained at a resolution of some 50 nm revealed areas of differing K concentration (60 - 180 mmol). These regions may correspond to dendrites, axons and and glial cells. Regions containing calcium were found with concentrations in the range 20-50 mmol, and these may correspond to organelles involved in calcium regulation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10184-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Physical Chemistry of Biological Macromolecules

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

Marc S. Lewis Research Chemist BEIB DRS

COOPERATING UNITS *(if any)*
LVR/NEI, LB, NIDR, SNB/NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.9	0.9	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to study the physical properties of a wide variety of biological macromolecules with the goal of correlating these properties to the structure and function of the macromolecules. The emphasis is on the thermodynamics of the interactions of these macromolecules and on their molecular size and shape. Analytical ultracentrifugation and mathematical modeling are the principal research techniques used.

The studies on the binding of plasminogen by fibrinogen described in the 1983 report have been published. Studies currently in progress in this area deal with the association of plasminogen with plasmin inhibitor, with the association of plasminogen with the D and E fragments of fibrinogen and with the association of fibrinogen with plasma Factor XIII.

Studies on the association of the A and B chains of reduced ricin indicate that the formaion of the AB complex is reversible and that the complex undergoes further reversible self-association to form polymers up to octomer. The temperature dependence of these reactions indicates that they are entropically driven, suggesting strong hydrophobic interaction between the chains.

Studies on the retinoid-binding protein from the interphotoreceptor matrix of the retina of macaque monkeys demonstrate that this is a significantly asymmetrical, hydrophobic glycoprotein with a molecular weight of 106,000.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10185-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Interventional Catheter Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

John W. Boretos, Physical Scientist, BEIB, DRS

Others:

John Doppman, M.D.	Radiologist	CR, CC, NIH
Edward Oldfield, M.D.	Neurosurgeon	NINCDS, NIH
Robert L. Dedrick, Ph.D.	Chem. Engr.	BEIB, DRS, NIH

COOPERATING UNITS *(if any)*
CR, CC, NIH; NS, NINCDS, NIH,
BEIB, DRS, NIH

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.4	0.7	0.7

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of the project is to develop a catheter system for interventional radiology which is capable of traversing small and branching blood vessels (i.e. 1.5 to 4.0 mm) to reach the proximity of tumors and to administer chemotherapeutic drugs to these tumors in a controlled manner. A major obstacle to effective treatment is thought to be mal-distribution of the drug at the site due to inadequate mixing with the blood. A multi-lumen micro-catheter, which is propelled and directed through these small blood vessels via jets of fluid emanating from its distal end, has shown promise for negotiating heretofore difficult to reach areas. The catheter is controlled by an adjustable pressurized manifold operated by a joy stick. Provisions for on-line switching from a radiopaque contrast solution to the drug is provided at the manifold. The contrast agent serves as the propelling fluid as well as providing visual identification of the movement and location of the catheter. While fluid turbulence generated at lower pressure by the drug emanating at retrograde angles from the tip of the catheter adds significantly to the mixing of the drug within the blood stream. Animal tests have substantiated the feasibility of the catheter system for clinical use. A transparent model of the vascular network simulating blood flow of a pulsatile nature was designed to evaluate the efficiency of the jet flow at various delivering rates. Surfaces of the catheters have been modified with bonded hydrogels to reduce drag through conventional sheaths and further acts to minimize clotting on the surfaces. A radiopaque marker at the tip of the catheter can be readily located by fluoroscopy.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10186-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Intravascular Implant Capsule

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*
John W. Boretos, Physical Scientist, BEIB, DRS

Others:

Milton Brightman, Ph.D.	Lab Chief	LNNS, NINCDS
Peter Bungay, Ph.D.	Chemical Engineer	CES, BEIB, DRS
Robert L. Dedrick, Ph.D.	Chemical Engineer	CES, BEIB, DRS

COOPERATING UNITS *(if any)*

LNNS, NINCDS,;CES, BEIB, DRS, NIH.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.3	0.7

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to develop a capsule to serve as an aid to in situ implantation of multiple tissue fragments into the fourth ventricle of rats for the study of neuronal growth and ultimately, to reconstruction of severed neurological circuits. The capsule shall further serve as a mechanical constraint to maintain the tissue fragments in registration and in close juxtaposition while at the same time providing for angiogenesis from the overlying cerebellum. Various polymeric capsules of one millimeter diameter were developed having a range of dissolution characteristics based on methyl cellulose (demethyl ether) and methyl cellulose crosslinked with polyfunctional resins combined with crosslinked and non-crosslinked collagen. The capsules exhibited sufficient initial rigidity for ease of loading of the tissue fragments and insertion into the fourth ventricle, yet immediately became soft in cerebral fluid. Only materials with a proven history of biocompatability were used. Dissolution times could be varied from 30 minutes to 8 hours in increments of 30 minutes depending upon the degree of crosslinking selected. The presence of the collagen added a plasticizing effect to the polymer system and provided a pseudo-fibrous network once the polymer dissolved. This network remains for extended periods and may be yeneficial in supporting and confining the tissue fragments beyond the initial stages of growth. Preliminary studies showed the capsules to be tolerated by the animals and some evidence that conditions in the fourth ventricle are suitable for neuronal growth.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10187-01 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Mixing During Intra-Arterial Infusion via Catheters

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

R.J. Lutz DRS, BEIB
J. Boretos DRS, BEIB
E. Oldfield NINCDS IR SN
J. Doppman CC DR
D. Miller CC DR
R. Pflueger DRS, BEIB
C. Thompson DRS, BEIB

COOPERATING UNITS *(if any)*

NINCDS
CC

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Chemical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.25	.75	.5

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Intra-arterial chemotherapy offers an alternative to systemic (iv) chemotherapy for localized neoplasms. Infusion of chemotherapeutic agents directly into the arterial supply of the neoplasm allows, under the proper circumstances, higher local tissue concentrations without a corresponding increase in systemic toxicity. Intra-arterial infusion rates are commonly in the range of 2 to 5 ml/min through a #5 or #7 French catheter. Results of such infusion have been varied and frequently suggest the possibility of preferential drug perfusion into local sub-regions of target tissue at position distal to the point of infusion. Often, some regions show areas of no drug effect, while other areas exhibit acute toxic responses. The suggestion has been put forward that fluid streaming from the catheter tip during infusion and, thereby, the absence of adequate drug mixing in the efferent blood supply to each arterial branch of the target tissue is one possible cause for the deliterious effects of this treatment modality. The aims of this project were to assess the degree of mixing of solutions infused from catheters into artery-like vessels, and to gain some insight into the fluid-mechanical factors that influence the mixing process. By means of model experiments, we have demonstrated that streaming can occur when infusion rates are too slow for the respective arterial size or arterial flow rates, and that drug solutions streaming at low infusion rates can advance preferentially into specific distal arterial branches. Mixing can be enhanced in numerous ways. e.g. by employing greater infusion rates, or by redesigning the catheter tipes to use "jet" infusion of drug solution transverse to the perfusing blood flow.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10188-01 BEI

PERIOD COVERED
February 1, 1984 to September 30, 1984

TITLE OF PROJECT *(80 charecters or less. Title must fit on one line between the borders.)*
Drug Transport in Brain

PRINCIPAL INVESTIGATOR *(List other profassionel personnel below the Principel Investigator.) (Name, title, leboretory, and institute affiliation)*

P.F. Morrison	Physical Scientist	BEIB, DRS
R.L. Dedrick	Chief, ChE Section	BEIB, DRS

COOPERATING UNITS *(if any)*
Surgical Neurology Branch, NINCDS, NIH (E.H. Oldfield)

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.7	0.7	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Concentration profiles of cis-platin in the cortex and cerebellum of the rat were analyzed with the intent of determining transport and reaction rate parameters. These parameters are needed to prospectively model various tumor treatment modalities for expected efficacy.

A reaction-diffusion model was formulated for cis-platin infusion from point and near-point sources. Both infinite and finite spherical transport regions were modeled, the latter to demonstrate that drug flow into the cerebral spinal fluid is of secondary importance. It was shown that the experimental concentration profiles corresponded to steady state conditions, and could be modeled by simpler steady-state mathematics.

Convection due to diluent flow from the infusion cannula was added to the reaction-diffusion model. Steady-state analysis showed that convection substantially modified the concentration profiles only over the first millimeter from the cannula tip.

More realistic geometry was introduced modelling the cerebellum as a prolate ellipsoid. Average total Pt concentrations for sections across this ellipsoid were fit to corresponding experimental tissue section data. The resulting fit, constrained by an independent measure of infusate recovery, provided estimates for cis-platin capillary permeability (9.03×10^{-7} cm/sec) and reaction rate (.005/min). The tissue diffusion constant was estimated as $1.9 \times 10\text{-}6$/sec, similar to creatinine due to the small hydrodynamic radius of cis-platin. The permeability is within the range predicted from octanol-saline partition coefficient/permeability correlations. The reaction rate compares with values reported for other tissues.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10189-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Cancer Risk Estimation

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

P.F. Morrison	Physical Scientist	BEIB, DRS
Cheryl Daniels	Chemical Engineer	BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Probabilistic analayses were performed to assess the effects of time variant exposure to carcinogen on cancer risk estimates.

Equations were formulated from several statistical models of cancer that allow one to determine the effects on risk estimates of (1) a time-varying toxic agent concentration and of (2) a migrating exposed population. The incidence models examined included the one-hit, multihit, and Weibull models. Present results show that the same risk estimates are obtained from the one-hit and multihit models when either the time-averaged dose or the fully time-dependent dose is used. The Weibull model requires that time-dependence be carried through the risk estimation procedure or else order of magnitude errors may occur (such as for the 30 year arsenic risk estimate when exposure actually occurs only over a third of this time). Migration was described by a first order partial differential flow model and was coupled to the incidence models via a residence time distribution formalism. Failure to include such a description of population migration results in both multihit and Weibull models overpredicting estimated risk, e.g. a Weibull model applied to arsenite toxicity will overpredict the incidence of skin cancer by ten-fold if an out-migration rate of 12% per year is ignored.

In addition, the multistage model for an arbitrary number of stages has been solved for constant concentration exposure. In turn, this multistage model along with multihit and Weibull models, was used to recast the form of cancer incidence expected at the cellular level to that expected at the organ level, the correct form to use when fitting to animal dose-response data.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10190-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Vessel Tortuosity and Vascular Resistance

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, end institute affiliation)*

R.S. Chadwick, Biomedical Engineer, BEIB
D. McGuire, Mathematician, BEIB
D. Goldstein, Senior Investigator, EHL, NHLBI
H. Kaiser, Chief EHL, NHLBI

COOPERATING UNITS *(if any)*
NHLBI, Endocrine - Hypertension Laboratory

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.35	.25	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This is a combined theoretical and experimental study designed to assess the importance of vessel tortuosity as a determinant of peripheral vascular resistance. An apparatus was designed and built to measure the relative hydrodynamic conductance of a machined tortuous tube. A range of physiological Reynolds numbers was obtained with aqueous solutions of glycerol. Theory relates the findings for a single tube to the input resistance of a vascular tree.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10191-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Continuous Optical Monitoring for Bacterial Cultures

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

G.M. Maxwell, Staff Fellow, BEIB, DRS
Ernst Freese, Chief, LMB, NINCDS

COOPERATING UNITS *(if any)*
LMB, NINCDS

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.2	

CHECK APPROPRIATE BOX(ES)

- ☐ (a) Human subjects
  - ☐ (a1) Minors
  - ☐ (a2) Interviews
- ☐ (b) Human tissues
- ☒ (c) Neither

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Several routine measures in molecular biology involve monitoring and/or controlling the population density of bacterial colonies grown in liquid medium by withdrawing samples and measuring turbidity. The purpose of this project is to develop a system to continuously monitor cell population by measuring associated changes in optical properties of the culture.

Current work is aimed at determining the feasibility of such techniques for short term study (8 hours). Current and future effort will be directed at determining and improving the long term stability (several days) of the transducer, improving the noise characteristics of the system, and developing the capability for simultaneous monitoring of multiple channels (32).

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10192-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Temperature Monitor for EM Induced Hyperthermia

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

G.M. Maxwell, BEIB, DRS
R. Levin, BEIB, DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project was to develop the associated electronics for multiple EM compatible commercially available temperature probes used to monitor the temperature in a hyperthermic phantom. A prototype system was constructed and, following testing and modification, a 16 channel system was constructed. Final testing and calibration are currently being performed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10193-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Development of Toposcopic Catheter for Clinical Gastroenterological Use

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

D.R. Shook, Biomedical Engineer. BEIB,DRS

COOPERATING UNITS *(if any)*
Naval Hospital Bethesda, Naval Medical Command, National Capital Region. USN (E.L. Cattau, T.J. Spurling); Esophogeal, Gastric and Colonic Diseases, Digestive Diseases and Nutrition Division, NIADDKD (K.J. Vener).

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☒ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The unique characteristics of the toposcopic catheter have suggested its application in the gastrointestinal system. The operation of the catheter promises to facilitate the catherterization of the pancreatobiliary ducts through the Papilla of Vater. An initial series of patients has undergone routine endoscopic retrograde cholanopancreatography (ERCP) using the topocatheter for contrast infusion. An extensively modified topocatheter is passed through an appropriately positioned endoscope. The catheter tip is placed within the ampulla, and the toposcopic element is everted. In basic ERCP, contract medium is then injected for appropriate diagnostic procedures. In addition, the topocatheter's ability to atraumatically negotiate small, tortuous ducts, is being applied to catheterization of remote pancreatic ducts for sampling of pure secretions, and of the cystic duct, for sampling and possible infusions for dissolution of gall stones.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10194-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Optimized Polymer Processing for Advanced Catheter Development

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

D.R. Shook, Biomedical Engineer, BEIB, DRS
B. Bourin, Guest Researcher, BEIB, DRS

COOPERATING UNITS *(if any)*
Diagnostic Radiology, CC (J.L. Doppman); Esophogeal, Gastric and Colonic Diseases, Digestive Diseases and Nutrition Division, NIADDKD (K.S. Vener)

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering Section,

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.6	0.5	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Advanced techniques of plasticating extrusion can produce materials of optimized anisotropic properties and very fine dimensional characteristics. Availability of such materials then supports development of unique polymeric medical devices, such as the toposcopic catheter. Unique polymer resins are first characterized specifically for extrusion characteristics and predictive models of rheological behavior are constructed. Die designs can now be implemented to take advantage of unique polymer character and to overcome the most critical processing difficulties. The models way also be used to eliminate certain polymers from consideration. Current efforts are to optimize the topocatheter material for maximally safe operation and to allow development of the topocatheter for arterial dilatation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10195-01 BEI

PERIOD COVERED

April 1984 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Fluoroimmunoassay Apparatus

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C. Wooten	Electronic Engr.	BEIB, DRS
W.S. Friauf	Ch., EEES	BEIB, DRS
R.L. Berger	Physicist	LTD, NHLBI
G. Hemphill	Electronic Tech.	BEIB, DRS

COOPERATING UNITS *(if any)*

CDC, Atlanta

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.4	0.3	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

New rare earth chelate fluorescent probes, with a decay time constant much longer than the background decay time-constant of typical organic materials offer the potential of a great improvement in sensitivity by appropriate timing of the response. However, to rival radioimmunoassay methods the required sensitivity improvement is so great that overload recovery of the fluorescence detector is a major problem. Extensive past work on this problem is largely inapplicable to the very low speed and level requirements of this situation. Consequently initial effort is being applied to determining the optimum fluorescence detection device and ancilliary signal overload limiting circuitry. Problems related to the fluorescent probe at extremely low sample concentrations will be studied in collaboration with CDC, which is interested in this approach as another tool for AIDS research. Finally an evaluationn of the details of excitation, optical filtering, and digital signal processing will be carried out and optimized.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10196-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Systems for Visual Response Testing

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C. Wooten	Electronic Engineer,	BEIB, DRS
P. Smith	Visiting Scientist,	BEIB, DRS
R. Nakamura	Investigator	LPD, NIMH
R. Phillips	Investigator	DCBR, NIMH

COOPERATING UNITS *(if any)*
NIMH

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, National Institutes of Health, Bethesda, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.7	0.5	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Many behavioral studies and EEG activity studies use visual stimuli to elicit a response and then use a reward system to encourage that response.

One particular system is used to measure monkey responses to transiently displayed pattern stimuli. An image is drawn on a CRT screen from computer memory, it is then shuttered by an electro-optic element for viewing times down to 5 ms and can therefore provide a repetition rate of 10 frames per second. A lens assembly including the electro-optic element is mounted in a housing suitable for projection of a video CRT image onto a viewing screen. Computer input to a control box provides a predetermined voltage to the electro-optic element which causes it to rotate the plane of polarization of the transmitted light by 90° and shutter it. In conjunction with this testing system, a water reward system was developed to provide the monkeys with a controlled dosage of water according to their response or non response to visual images.

Another visual stimulus system involves the use of a slide projector to project the images on a ground glass screen directly in front of a monkey who is tethered to a chair to pick up EEG recordings. A capacitive touch panel is provided for positive response to the image and a resistive touch panel is provided for the negative response.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10197-01 BEI

PERIOD COVERED
October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Effect of Experimental Parameters on Derived SSD's

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.R. Swyt Physical Scientist BEIB DRS
R.D. Leapman Special Expert BEIB DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electron Beam Imaging & Microspectroscopy - Office of the Chief

INSTITUTE AND LOCATION
DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The derivation of a single scattering distribution (SSD) from a collected electron energy loss (EELS) plural scattering spectrum (PSS) may fail if the collected spectrum incorrectly represents the amount of plural scattering. Errors in elemental edge identification and quantitation for the thicker (greater than about 1000A in carbon for 100keV beam energy) biological specimen are then compounded.

In order to determine the experimental condition which is the source of the particular error in the collected spectrum, software was written to generate plural scattering spectra from a given single scattering distribution. These spectra weregenerated with modifications to simulate the effects of various experimental conditions that cause the amount of plural scattering to be incorrectly estimated in a collected spectrum.

The derived incorrect SSD's were catalogued with the experimental condition that is the source of the particular distribution. This catalogue will help the investigator to identify and correct the experimental conditions which have modified the collected plural scattering spectra. This should yield greater accuracy in edge identification and quantitation.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10198-01 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Concurrent Dynamic Focussing of Two WDS Spectrometers

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: C.R. Swyt Physical Scientist BEIB DRS
Other: C.E. Fiori Physical Scientist BEIB DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electron Beam Imaging and Microspectroscopy Group

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The Cameca MBX Microprobe has been interfaced to the DEC PDP 11/60 computer controlled Hitachi H700H TEM-STEM elemental imaging system. Elemental x-ray image acquisition is now possible on the microprobe with either the energy dispersive (EDS) or wavelength dispersive (WDS) detectors. In many cases the WDS detectors are preferred to the more efficient EDS detector because of their superior resolving power and high peak to background ratio. Also for many speicmens an image magnification of 100x or 200x is most informative. At these magnifications the large area (1mm at 100x) which is digitally scanned results in WDS spectrometer defocussing relative to the source of the x-rays and thus artifactual variation in pixel intensity across the elemental images.

In order to overcome the defocussing problem, software to dynamically focus both spectrometers in synchronism with the scanned electron beam was written. The 11/60 computer controls two Canberra Industries Axis Positioners using their Model 6726 Telecomputer Interface as the executive link. The spectrometer crystals are driven to the focussed positions for each beam location by controlling two positioner stepping motors. The focussed positioner settings are calculated from calibration files of beam coordinates at image limits and corresponding focused spectrometer settings obtained with standard specimens for each element of interest.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 RS 10199-01 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Derivation of Single Scattering Distributions from EELS Spectra

PRINCIPAL INVESTIGATOR *(List other professionel personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.R. Swyt Physical Scientist BEIB DRS
R.D. Leapman Special Expert BEIB DRS

COOPERATING UNITS *(if any)*

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electron Beam Imaging and Microspectroscopy

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.2	.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Plural scattering effects in an electron energy loss spectra (EELS) acquired from biological sections of thickness greater than about 1.0 mean free path (600 A at 100keV beam energy for carbon) may lead to errors in elemental edge identification and quantitation.

A large FORTRAN software package has been written which allows the investigator to derive the single scattering distribution (SSD) from a collected plural scattering spectrum (PSS). Formulations for the SSD were developed for spectra with small dynamic range and low energy loss edges and for spectra requiring amplifier gain change but with edges that can be background subtracted. Algorithms were then developed for each case. The required deconvolutions are performed using a real fast Fourier transform (FFT). The fourier coefficients (FC) of the SSD may be extracted from the FC of the total PSS using a logarithmic formulation or from the FC of the background subtracted core edge distributions divided by the FC's of the low loss distribution.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER: Z01 RS 10200-01 BEI

PERIOD COVERED

October 1, 1983 to September 30, 1984

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Cell Culture Incubator

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

C.P. Mudd Biomedical Engineer ACES, BEIB, DRS
H.W. Tipton, Mech. Engr. Tech, ACES,BEIB, DRS
J. Robbins, Research CC

COOPERATING UNITS *(if any)*

CC

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering Section

INSTITUTE AND LOCATION

DRS, National Institutes of Health, MD 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither

☐ (a1) Minors

☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This project is set up to proceed in two phases. In phase 1, a standard incubator will be modified to allow uniform, low level irradiation of cell cultures while maintaining control of temperature, humidity and CO_2. The cell holders will be mounted on a carousel and rotated to ensure uniform exposure. The top of the incubator will be removed and a lexan top used to allow the passage of radiation.

Based upon the results in phase I, a larger version will be constructed for phase 2.